

officials had reviewed the study and wanted to pursue participation. Attorneys with the city and county also have approved the trial, he said.

“We’re at the point with the entities to move forward with the education component,” Bradford said.

He said his department has a history of being involved with cutting-edge research.

Moncure said he wanted Douglas County’s participation, in part, because of the high volume of traffic along Kansas Highway 10 headed to the Kansas City metropolitan area.

The KU Medical Center’s Human Subjects Committee is scheduled to review public input from Wyandotte, Leavenworth and Johnson counties on Oct. 11. If it is satisfied with support, it will approve the use of PolyHeme starting in November.

Moncure said if a meeting can be scheduled in Lawrence — probably at the Lawrence Public Library — before then, Douglas County’s participation could be approved at the same meeting. He said little opposition had developed in other counties or at other sites involved.

Additional public education will occur after community approval, Moncure said.

“We’ll be hitting the news, the airwaves, print, taking out ads after getting approved from our (Human Subjects Committee),” he said.

**LJWORLD.COM**  
LAWRENCE JOURNAL-WORLD

## **Synthetic blood meeting to be held Monday**

Friday, October 7, 2005

A public meeting to discuss the proposed clinical trial for PolyHeme, a synthetic blood product designed for use in trauma patients, has been set for 7 p.m. Monday in Kansas University's Memorial Union, 1301 Jayhawk Blvd.

The meeting, organized by KU Medical Center, will be in Alderson Auditorium on Level 4 of the Union.

There will be a brief overview of the proposed clinical trial and a question and answer session. Attendees will be asked to fill out a form expressing their views on the project.

KU is one of 21 study sites across the country involved with the Food and Drug Administration trial of PolyHeme, a blood substitute manufactured by Northfield Laboratories in Evanston, Ill.

Officials with Lawrence-Douglas County Fire & Medical have approved their participation in a clinical trial that would use the product to treat critically injured trauma victims.

Posted on Fri, Oct. 28, 2005

Ambulance crews would have used artificial blood in Johnson County

## Role in research rejected

By FINN BULLERS and ALAN BAVLEY  
The Kansas City Star

A national study that could revolutionize the treatment of trauma victims will move forward.

But without Johnson County.

Annabeth Surbaugh, the county's top elected official, cast a tying vote that barred the county's Med-Act ambulance service from participating in an ongoing study conducted by University of Kansas Medical Center to test whether artificial blood used at the scenes of accidents could help save more lives.

The County Commission's support would have given emergency crews implied consent to treat trauma patients with artificial blood without their approval.

Surbaugh said she came to Thursday's meeting prepared to support the study but changed her mind when she learned the details of how it would be administered.

"I didn't know enough to vote yes, so I voted no," Surbaugh said after the vote. "Perhaps this is because of my lack of medical understanding."

The study — approved in Wyandotte, Douglas and Leavenworth counties — will continue despite the no vote in Johnson County.

A commissioner who voted for inclusion in the study said the vote sent a troubling message as Kansas leaders bank on an emerging life sciences initiative to spark a new growth industry in the Sunflower State.

Earlier this month, Surbaugh and her colleagues sang the praises of a new life sciences research park that Gov. Kathleen Sebelius envisioned at the former Sunflower Army Ammunition Plant near De Soto.

"But it troubles me in looking ahead," Commissioner Dolores Furtado said after the vote. "How can we celebrate the potential of a research park at Sunflower dedicated to bioresearch" while sending an anti-science message?

"It has to have a detrimental impact on any bioresearch firm that may consider locating in Kansas," said Furtado, professor emeritus of microbiology at the University of Kansas Medical Center.

Also citing the county's biotech future, Commissioner John Toplikar voted against the study. Participating would lead the county down the wrong road as a Kansas 10 "biotechnology corridor" begins to emerge between the Stowers Institute in Kansas City and the University of Kansas in Lawrence, Toplikar said.

"If we approve this study, what study is next?" he asked.

He said the study "takes away the basic human rights" of people by enrolling them in a study they can't decline without

**CONTINENTAL.COM.**  
**MORE POWER TO YOU.**  
Manage all your travel  
at [continental.com](http://continental.com).

**SEARCH FOR FLIGHTS**

FROM:

TO:

DEPART:

RETURN:

**Continental Airlines**

MORE NEWS FROM **TOPICNET**

- Microbiology
- Biology
- Science

wearing opt-out wristbands.

The study is expected to begin on schedule in mid-November, even without Johnson County's participation, KU Medical Center spokesman Dennis McCulloch said.

"We're disappointed, but the project will go on, and we'll still be part of this national research," McCulloch said.

McCulloch said the medical center was surprised by the continuing doubts about the study raised by the County Commission.

"We were kind of stunned by the questions," he said. "We think we had answered their questions."

Since early last year, an experimental blood substitute known as PolyHeme has been given to hundreds of U.S. trauma patients suffering life-threatening blood losses at accident scenes.

PolyHeme has been tested extensively in hospital emergency rooms. More than 20 medical centers nationwide are participating in the ambulance study. But other hospitals have declined to participate.

Researchers face sticky ethical questions on whether trauma patients unable to make informed decisions about their treatments should be transfused with PolyHeme without their consent. Under normal circumstances, that's forbidden.

But it does happen.

"There are areas of research in which new medications do get used without traditional informed consent," said Gary Pettett, a program associate of the Center for Practical Bioethics and director of the office of research integrity at Children's Mercy Hospital.

These situations include research involving young children where the approval of their parents is sought and emergency care where patients are incapacitated.

"If we're ever going to improve the kind of care available in emergency settings, we're going to have to be able to study it like this," Pettett said.

Studies without informed consent can be ethically justified, he said, if an experimental treatment is likely to benefit patients and if its risks have been minimized.

"It sounds to me the (PolyHeme) study has passed muster as far as it can in the emergency setting," he said.

"But you have to be willing to accept community assent as an ethical substitute for informed consent. If that is still an ethical dilemma for (the County Commission), I don't think there's any way around it for them. I think you have to honor that decision."

T.J. Clark of Olathe told commissioners Thursday he did not want them to make medical choices for him.

"This is an experiment," said Clark, a local radio talk show host. "We need to scream it from the rooftop."

The message to the public is that "your County Commission has decided you're going to be a guinea pig," he said.

Furtado chalked up the vote to pre-election posturing.

"Annabeth took me by surprise," Furtado said. "I think it (her vote) is political. She is serving the conservative base —

be it so they don't mobilize a candidate to run against her or be it to win the race. I don't know."

Surbaugh, who has announced a bid for another four-year term as county chairwoman next fall, denied the allegation.

"My decision was not a political decision," she said.

Had she been given more time to study the issue she said she may have drawn a different conclusion. The commission had already delayed its vote one week.

Commissioner Dave Lindstrom also voted against participating in the study, saying he was concerned that participants would continue to receive PolyHeme even after real blood was available at the hospital.

Commissioner Doug Wood abstained from voting, saying, "I do not want to substitute my judgment for those of my constituents."

Commissioners Furtado, Ed Peterson and John Segale supported the study.

The vote reflects the conservative/moderate split that surfaced during this year's budget deliberations.

Segale said Thursday's debate got sidetracked by questions of morality and ethics.

When emergency responders make life-or-death decisions to pump saline into trauma victims to stabilize blood pressure, they don't ask for permission, he said. This study is to decide whether to take a calculated risk to save lives — and it is worth taking, Segale said.

Ted McFarlane, director of the ambulance service, said a review of 75 Johnson County trauma cases transported to KU Medical Center in the last year showed no case that would have qualified for inclusion in the study.

---

### **What is PolyHeme?**

■ *It is produced from human blood and retains blood's ability to carry oxygen to body tissues. PolyHeme is more practical than blood for use on ambulances because it's easier to store and has a longer shelf life than blood. And it can be given to people without matching blood types.*

---

### **The study**

■ *More than 400 patients have been enrolled in the ambulance study. KU Medical Center expects to contribute about 40 patients to the study. It will continue until 720 patients are enrolled.*

■ *Half of these trauma patients will receive PolyHeme, the rest conventional therapy with intravenous fluids.*

■ *Johnson County was expected to supply about four of those patients by ground transport and two to three times that number by air ambulance. Without Johnson County, it will take scientists longer to get their research numbers.*

**QUESTIONS AND ANSWERS  
POLYHEME® TRAUMA TRIAL  
THE UNIVERSITY OF KANSAS HOSPITAL  
THE UNIVERSITY OF KANSAS MEDICAL CENTER**

**Why is this study being conducted?**

*To evaluate the safety and efficacy of PolyHeme® in treating severely injured and bleeding patients, starting at the scene of injury, and to assess a potential survival benefit.*

**What is the title of this study?**

*A Phase III, Randomized, Controlled, Open-Label, Multicenter, Parallel Group Study Using Provisions for Exception from Informed Consent Requirements Designed to Evaluate the Safety and Efficacy of Poly SFH-P Injection [Polymerized Human Hemoglobin (Pyridoxylated) PolyHeme®] When Used to Treat Patients in Hemorrhagic Shock Following Traumatic Injuries Beginning in the Prehospital Setting*

**What is PolyHeme®?**

*PolyHeme® is a temporary oxygen-carrying red blood cell substitute made from human blood. PolyHeme® requires no cross-matching, and therefore is compatible with all blood types. PolyHeme® is manufactured using steps to reduce the risk of viral transmission. It has a shelf-life of over 12 months.*

**What is the design of this study?**

*Patients in "hemorrhagic shock" will begin to receive either saline (salt water), which is the standard of care (control), or PolyHeme (investigational treatment). Treatment will begin before arrival at the hospital, either at the scene of the injury or in the ambulance, and continue during a 12 hour postinjury period in the hospital.*

*During this study Polyheme® is compared to standard of care, saline (salt water) in the pre-hospital setting and blood in the hospital.*

*At the site of the injury, half of the subjects (like flipping a coin) receive Polyheme®, half receive standard care (saline). It is given by emergency medical personnel before reaching the hospital (may be up to 60 minutes).*

*Upon arrival to the emergency room, subjects receive Polyheme® or standard care (blood). Subjects that received Polyheme® at the emergency site continue to receive Polyheme® in the hospital instead of standard care (blood). PolyHeme® is given for up to 12 hours or 6 units of PolyHeme. Standard care (blood) will be given (if needed) after 12 hours or 6 units of PolyHeme ®. Patients who originally receive the saline solution in the field will receive standard care (blood) upon arrival to the emergency room (standard of care).*

**What is hemorrhagic shock?**

*A condition in which a patient has experienced massive blood loss. Shock is a life-threatening condition that might include:*

- *Dangerously low blood pressure*
- *Internal organs not receiving enough oxygen and have difficulty functioning, which could lead to death*

**Why is there a need for improvement in the way trauma patients are treated now?**

*Trauma is the leading cause of death among Americans under the age of 45. Currently the only available treatment for hemorrhagic shock, when blood is not available, is the infusion of a solution that does not carry oxygen such as saline (salt water). Therefore, when blood is not immediately available, use of an oxygen carrier such as PolyHeme® may restore sufficient circulating levels of hemoglobin and potentially improve patient survival.*

*There are also risks associated with large infusions of donated blood in trauma patients, including an increase in immune function which may cause failure of vital organs and death in some patients who receive transfusions [A. Sauaia et al., Archives of Surgery (1994), Volume 129:39-45]. In a controlled Phase II trial in hospitalized trauma patients, higher levels of immune markers were seen in patients receiving blood transfusions as opposed to those who received PolyHeme® [E. E. Moore, Journal of American College of Surgeons (2003), Volume 196 (1)].*

**What is the current standard of care? How are trauma patients usually treated?**

*Bleeding patients are given a solution, such as saline, at the scene or in the ambulance to raise blood pressure. When patients arrive at the hospital, they are given Type O blood, if needed immediately, and later receive cross-matched blood, when available, if they continue to need blood transfusion.*

**Who is eligible for the study?**

*Patients who have lost a large amount of blood and are in shock  
Patients who are at least 18 years old  
Patients who have sustained severe injuries*

**Who will be excluded from the study?**

*Women who are obviously pregnant  
Patients with severe brain injuries  
Patients who require CPR to maintain their heartbeat  
Patients with "unsurvivable" injuries  
Patients who are known to object to blood transfusions  
Patients who are known to refuse resuscitation*

**How many patients will be enrolled in the study?**

*A total of 720 patients will be enrolled in the study; 360 patients in the control group and 360 patients in the PolyHeme® group.*

**Has enrollment begun anywhere?**

*Currently, enrollment is underway at 17 Level I trauma centers across the United States. A list of those centers is available at [www.clinicaltrials.gov](http://www.clinicaltrials.gov). The FDA has approved this study as well as a total of 22 Institutional Review Boards. One IRB did not approve the study.*

**How will patient safety be assured in this trial?**

*An Independent Data Monitoring Committee, consisting of independent medical and statistical experts, is responsible for periodically evaluating the safety data from the trial and making recommendations relating to the continuation or modification of the trial protocol to minimize any risks to patients. The protocol includes four planned evaluations that occur after the first 60, 120, 250 and 500 patients have been enrolled and monitored for a 30-day follow-up period.*

**What has been the experience with the study since it has begun?**

*The Independent Data Monitoring Committee (IDMC) has reviewed the safety data on mortality and serious adverse events from the ongoing trauma study after the first 60, 120 and 250 patients were enrolled and followed for 30 days. After these three safety looks, the Committee recommended that the study continue without any change. In addition, at the 250 patient look, the IDMC conducted an adaptive sample size determination as specified in the protocol. A blinded power analysis was performed to determine if any increase in the sample size of the study was necessary. The assessment was based on a comparison between the mortality rate predicted in the protocol and the observed mortality rate in the trial to date. The IDMC has concluded that no adjustment in the number of patients to be enrolled in the study is required.*

**How many units of PolyHeme® have been given to patients previously?**

*Northfield has experience with PolyHeme® in patients with acute blood loss in trauma and elective surgery in the hospital setting, including those who have received up to 20 units (pints) containing 1,000 gm of PolyHeme®. The normal volume of blood in a human is 10 units (pints) containing 500 gm of hemoglobin. This means that up to two times the normal volume of blood in a human has been replaced by PolyHeme®. Some of these patients were kept alive while losing virtually all of their own blood during ongoing bleeding and receiving only PolyHeme® as replacement. Observations in these patients have suggested the life-sustaining potential of PolyHeme® in the treatment of urgent life-threatening blood loss and life-threatening hemoglobin levels [Gould et al, Journal of American College of Surgeons (2002), Volume 195 (4)].*

**What has been the safety experience with PolyHeme® in prior studies?**

*During the course of evaluation of any investigational product, both adverse experiences and serious adverse experiences can occur. These may be due to either the underlying condition of the patient, the treatment setting, or the investigational product itself. Both adverse experiences and serious adverse experiences have occurred in prior studies.*

*PolyHeme® was studied in one trial in patients experiencing planned acute blood loss while undergoing elective surgery for abdominal aortic aneurysm. The trial included a non-routine procedure called acute normovolemic hemodilution (ANH) in which a large quantity of the patient's own blood, up to 60%, is removed prior to the surgery, and is later replaced. The procedure in this study resulted in the infusion of large volumes of blood in addition to up to 6 units of PolyHeme® in the experimental group, while smaller overall volumes of blood alone were administered in the control group. Serious cardiovascular adverse experiences occurred more frequently in the PolyHeme® group. The patients in this study were older with more cardiovascular risk factors than those in the trials in trauma patients. It cannot be determined whether these findings are due to the more extensive ANH in the PolyHeme® group, to the reinfusion of more blood following surgery in the PolyHeme® group or to PolyHeme® itself.*

*In trauma patients, PolyHeme® has been rapidly infused during urgent life-threatening blood loss in sufficiently large quantities, up to 20 units (pints), to be considered well-tolerated in this patient population [Gould et al, Journal of American College of Surgeons (2002), Volume 195 (4)].*

**What is an exception from informed consent?**

*Patients are enrolled (put) in a clinical study without giving informed consent before being enrolled.*

### **Why was such an exception granted in connection with this study?**

*Patients are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence is necessary to determine the safety and effectiveness of particular interventions.*

*Participating in the study has the potential for of direct benefit to the enrolled patients, defined as an increase in survival, because:*

- *Patients are in a life-threatening situation that necessitates intervention*
- *Previous studies support the potential to provide a direct benefit to enrolled patients*
- *Risks associated with the use of the PolyHeme® are reasonable in relation to what is known about the patients' medical condition, the risks and benefits of standard therapy, and the risks and benefits of the proposed intervention*

*It is expected that patients will be unable to give informed consent because the extent of their injuries and the fact that they are in shock.*

*It is unlikely that there will be time to find and ask for consent from the patient's legally authorized representative (LAR) or to provide an opportunity for a family member to object to the patient's enrollment before beginning treatment.*

### **Who grants such exceptions?**

*The U.S. Food and Drug Administration (FDA) under regulations called 21 Code of Federal Regulations 50.24 specifies the conditions under which an exception from informed consent may be obtained. The Institutional Review Board (IRB) associated with each hospital approves its use locally.*

### **What if someone doesn't want to participate in this study?**

*If someone in the community would like to be excluded from participating in this study, an "opt out" wristband will be provided at no cost. If someone in the community is involved in a trauma and they are wearing the wristband they will not be placed in the study. Information regarding how to obtain the "opt out" wristband will be available on the KU websites: [www.kumc.edu](http://www.kumc.edu) and [www.kumed.com](http://www.kumed.com) or by calling the study coordinator, Suzanne Porras, R.N. at 913-588-4022.*

### **What if a patient wants to stop their participation in the study?**

*Patients can withdraw from the study, without prejudice, at any time by notifying the investigator. If the patient is not competent to be making decisions about their participation, a family member does have the ability to request that the patient's participation be ended.*

### **Will patients still receive treatment if they don't want to participate in the study?**

*Patients will still receive the standard of care if they decline to participate in this study.*

### **What are the potential benefits of PolyHeme®?**

*PolyHeme® may increase the likelihood of survival after traumatic injury*

*The need for blood transfusion might be reduced*

*Patients might avoid a reduction in the function of internal organs that sometimes follows blood transfusion*

### **What are the potential risks of PolyHeme®?**

*Rash*

*Increased blood pressure*

*Kidney or liver damage*

*Transmission of hepatitis and HIV viruses  
Unforeseen happenings  
PolyHeme® may be less effective than blood*

*Some of these risks may lead to death.*

**How much will it cost patients to participate?**

*There is no charge to the patient to participate in this study. The costs of certain laboratory tests that are required will be paid by the study sponsor.*

**Will patients get paid to participate?**

*No, patients will not be paid to participate in this study.*

**Who is the manufacturer of PolyHeme®?**

*Northfield Laboratories Inc., Evanston, IL. For more information, visit [www.northfieldlabs.com](http://www.northfieldlabs.com)*

**###**

## PolyHeme® Trauma Trial

### Community Consultation

University of Kansas Hospital  
kumc.edu/polyheme or  
kumed.com  
3901 Rainbow Blvd, Kansas  
City, Kansas 66160  
September 21, 2005

## Clinical Investigator

Dr. Michael Moncure M.D.  
Principal Investigator  
913-588-7230

Human Subjects Committee  
913-588-1240

## Study Sponsor

### Northfield Laboratories Inc.

- Developer of the temporary oxygen-carrying red blood cell substitute called PolyHeme®
- Conducted multiple studies with PolyHeme over the past decade
- Most studies have been with injured trauma patients
- Company website: [www.northfieldlabs.com](http://www.northfieldlabs.com)

## Study Purpose

*To evaluate the life-sustaining potential of PolyHeme® when given to severely injured and bleeding patients in "hemorrhagic shock," starting at the scene of injury*

## What is Hemorrhagic Shock?

**Hemorrhagic:** massive loss of blood

**Shock:** life-threatening condition

- Dangerously low blood pressure
- Internal organs don't receive enough oxygen and have difficulty functioning
- Might lead to death

## Need for Improved Outcome

- The Center for Disease Control (CDC) lists trauma as the leading cause of death among Americans under age 45
- Thousands of trauma patients die each year
- Many of these patients die because the "standard of care" cannot reverse the damaging effects of hemorrhagic shock

## What is the Standard of Care?

*Represents the current treatment*

### *In the Ambulance*

The patient receives  
salt water  
(blood is not available)

### *In the Hospital*

The patient receives  
salt water  
and donated blood

## Standard of Care Limitations

### *In the Ambulance*

- Salt water does not carry oxygen, unlike blood
- Without enough oxygen, the body and its internal organs have difficulty functioning and can stop working (organ failure)

## Standard of Care Limitations

### *In the Hospital*

- Risks associated with large infusions of donated blood in trauma patients have been identified
- Increase in immune function, which may cause failure of vital organs and death, observed in some patients who have received transfusions<sup>1</sup>

<sup>1</sup>A. Savata et al., *Archives of Surgery* (1994),  
Volume 129:39-45

## What is PolyHeme®?

*A temporary red  
blood cell  
substitute  
that carries oxygen*

*In the acute setting, 1  
unit (pint) of  
PolyHeme is given in  
place of 1 unit (pint)  
of blood*



## What is PolyHeme®?

- Made from human blood
- Compatible with all blood types
- Immediately available
- Manufactured with steps to reduce the risk of viral transmission



## Why Use PolyHeme®?

- PolyHeme was developed to treat blood loss when blood is not available
  - Blood is not available in the ambulance
  - PolyHeme will be immediately available in the ambulance and carries oxygen
- PolyHeme can reduce the use of donated blood in the first 12 hours after injury, and might avoid potential organ failure

### Why Use PolyHeme®?

- There are risks associated with large infusions of donated blood in trauma patients<sup>1</sup>
- In a controlled Phase II trial in hospitalized trauma patients, higher levels of immune markers were seen in patients who received blood transfusions as compared to those who received PolyHeme<sup>2</sup>

<sup>1</sup>A. Savaia et al., *Archives of Surgery* (1994), Volume 129:39-45

<sup>2</sup>E. E. Moore, *Journal of American College of Surgeons* (2003), Volume 196 (1)

### PolyHeme® Experience

- PolyHeme has been studied in more than 300 individuals and 5 different clinical trials
- PolyHeme has been extensively studied in hospitalized trauma patients
- *PolyHeme has kept trauma patients alive when they have lost all of their own blood*

### Why Use PolyHeme®?

*To evaluate a potential improvement in survival of severely injured and bleeding patients*

### PolyHeme® Experience: Past

- Administered to patients with acute blood loss in the hospital setting
- Patients have received up to 20 units (pints) or 1,000 gm of PolyHeme®
  - Normal volume of blood in a human is 10 units (pints) or 500 gm of hemoglobin
- Some of these patients kept alive while losing virtually all of their own blood during ongoing bleeding and receiving only PolyHeme® as replacement.

### PolyHeme® Experience: Past

- Observations in these patients have suggested the life-sustaining potential of PolyHeme® in the treatment of urgent life-threatening blood loss and life-threatening hemoglobin levels

[Gould et al, *Journal of American College of Surgeons* (2002), Volume 195 (4)]

### PolyHeme® Experience: Past

- During the course of evaluation of any investigational product, both adverse experiences and serious adverse experiences can occur. These may be due to either:
  - the underlying condition of the patient
  - the treatment setting or
  - the investigational product itself
- Both adverse experiences and serious adverse experiences have occurred in prior studies.

### PolyHeme® Experience: Past

- One trial conducted in older patients undergoing elective surgery for abdominal aortic aneurysm that involved a non-routine procedure where up to 60% of their own blood was removed and later replaced.
- Serious adverse events, including cardiovascular, were observed.
- It cannot be determined whether due to experimental procedure or PolyHeme itself.
- Patients in this study were older with more cardiovascular risk factors than those in the trials in trauma patients.

### PolyHeme® Experience: Past

- In trauma patients, PolyHeme® has been rapidly infused during urgent life-threatening blood loss in sufficiently large quantities, up to 20 units (pints), to be considered well-tolerated in this patient population.

*[Gould et al, Journal of American College of Surgeons (2002), Volume 195 (4)]*

### PolyHeme® Experience: Current Trial

- 720 patients will be enrolled:
  - 360 patients in the control group
  - 360 patients in the PolyHeme® group
- Currently, enrollment underway at a 17 Level I trauma centers across the United States
  - A list of centers is available at [www.clinicaltrials.gov](http://www.clinicaltrials.gov)
- The FDA has approved the study
- 22 Institutional Review Boards have approved the study. 1 IRB has not approved the study

### PolyHeme® Experience: Current Trial

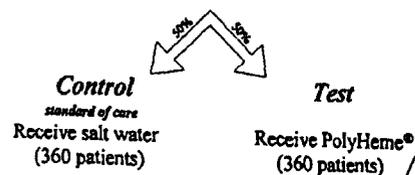
- An Independent Data Monitoring Committee set up to review mortality and serious adverse experiences after 60, 120, 250 and 500 patients have been enrolled and followed for 30 days
- Committee has reviewed the safety data on the first 60, 120 and 250 patients
- Committee has recommended that the study continue without any change

### PolyHeme® Experience: Current Trial

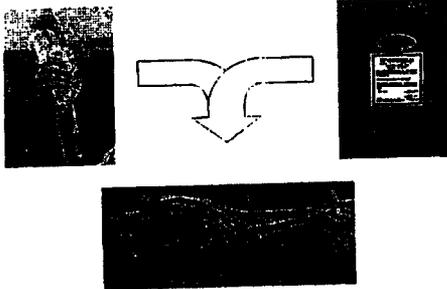
- At the 250 patient look, Committee conducted an adaptive sample size determination.
- Assessment was based on a comparison between the mortality rate predicted in the protocol and the observed mortality rate in the trial to date.
- Committee has concluded that no adjustment in the number of patients to be enrolled in the study is required.

### Trial Design: Before the Hospital

*Severely injured trauma patients will be assigned to either one of two groups by chance*



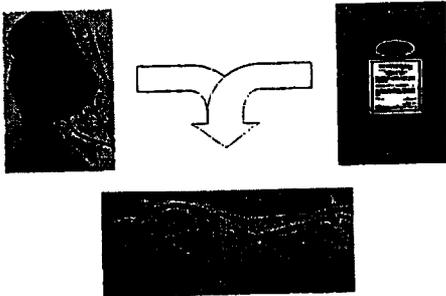
### Ambulance Infusion



### Trial Design: At the Hospital

- | <i>Control</i><br><i>Standard of Care</i>   | <i>Test</i>   |
|---|---|
| <ul style="list-style-type: none"><li>• Salt water for hydration</li><li>• Donated blood to boost oxygen levels</li></ul> | <ul style="list-style-type: none"><li>• Salt water for hydration</li><li>• PolyHeme® to boost oxygen levels</li><li>• Maximum dose of 6 units during first 12 hours</li><li>• Donated blood will be used thereafter</li></ul> |

### Hospital Infusion



### Hospital Infusion

- Patients in the test group will not receive donated blood (standard of care) in the hospital until either:
  - 6 units of PolyHeme have been given
  - Or, 12 hours have gone by after injury
- After 12 hours, the patients in the test group will receive donated blood as needed

### Who Would Be Included?

#### *Patients at risk of dying*

- Who have sustained severe injuries
- Who have lost a large amount of blood and are in shock
- Who are at least 18 years old
- Who are of either gender (male or female)

### Who Would Be Excluded?

- |   |  |
|---|--|
| <ul style="list-style-type: none"><li>• Patients who are obviously pregnant</li><li>• Patients who have severe head or brain injuries</li><li>• Patients who have "unsurvivable" injuries</li></ul> | <ul style="list-style-type: none"><li>• Patients who require CPR</li><li>• Patients with known objections to blood transfusions</li><li>• Patients with known orders not to resuscitate</li><li>• Patient with visible or identifiable method of objection (e.g. wearing exclusion bracelet)</li></ul> |
|---|--|

### Who Would Be Excluded?

- If someone in the community would like to be excluded from participating in this study, an "opt out" wristband will be provided at no cost. If someone in the community is involved in a trauma and they are wearing the wristband they will not be placed in the study. Information regarding how to obtain the "opt out" wristband will be available on the KU websites: [www.kumc.edu](http://www.kumc.edu) and [www.kumed.com](http://www.kumed.com) or by calling the study coordinator, Suzanne Porras, R.N. at 913-588-4022.

### FDA Review

- Northfield Laboratories received clearance to proceed with this study from the Food and Drug Administration (FDA)
- The FDA authorized the use of an exception from informed consent requirements for this study

### What is Informed Consent?

A process by which patients make informed decisions about participating in research studies

- Traditionally required for all research studies
- Research studies compare 2 treatments (standard vs. investigational)
- Doctors describe each of these potential treatments

### What is Informed Consent?

A process by which patients make informed decisions about participating in research studies

- Patients are informed of the potential risks and potential benefits associated with each of these treatments
- Patients choose whether to participate in the study

### What is Exception from Informed Consent?

*Patients are enrolled in a research study without giving their informed consent*

### How Can That Be?

A federal regulation (21 CFR 50.24), created in 1996, allows certain studies that meet the following criteria to use this exception

- *Patients' lives must be at risk*
- Available treatments are not satisfactory
- Patients are unable to give consent
- Potential risks are reasonable

### How Can That Be?

A federal regulation (21 CFR 50.24), created in 1996, allows certain studies that meet the following criteria to use this exception

- Participation in the research could provide a direct benefit (*increased survival*) to the patient
- The research could not be practicably carried out without an exemption

### Consent Safeguards

- If possible, the patient or a legally authorized representative (LAR) can give consent before the patient is enrolled in the study
- If consent cannot be obtained before enrollment, frequent attempts will be made to contact the patient's LAR and family to describe the study

### Consent Safeguards

*The patient, family members, or a legally authorized representative may decide to withdraw the patient at any time*

### Potential Benefits of PolyHeme®

- *Might increase the likelihood of survival*
- Can enhance the amount of vital oxygen in the patient's blood (prehospital setting)
- May avoid failure of vital organs (prehospital and hospital settings)
- Is compatible with all blood types
- Is immediately available
- Manufactured with steps to reduce the risk of viral transmission

### Potential Risks of PolyHeme®

- Rash
  - Increased blood pressure
  - Kidney or liver damage
  - Viral infection (HIV, hepatitis, etc.)
  - Unforeseen happenings
  - PolyHeme® may be less effective than blood
- Some of these risks may lead to death.

### Patient Protection

The Institutional Review Board (IRB) is a group of medical, scientific, and nonscientific members of the community

- Reviews all proposals for research on humans
- Assures patient safety
- Monitors community feedback

### Patient Protection

- The IRB will decide whether or not to allow this hospital to participate in the PolyHeme® trial
- An independent data monitoring committee is overseeing the trial to monitor the safety of the product
- The FDA is being informed of the trial's progress

### If We Participate...

- The results of the study will be revealed to the community after the trial has been completed
- Those who do not want to participate in the study can wear a special bracelet to exclude themselves

Questions  
or  
Comments?